DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 19-281/S-015

Pharmacia & Upjohn Company
Attention: Ms. Roma Thomas
Regulatory Manager
Regulatory Affairs – Marketed Products
7000 Portage Road
Kalamazoo, MI 49001-0199

Dear Ms. Thomas:

Please refer to your supplemental new drug application dated, May 14, 2001, received May 15, 2001, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for CYKLOKAPRON® (tranexamic acid) Injection.

This supplemental application proposes the following change to the package insert (PI): in the PRECAUTIONS section, the addition of a "Geriatric Use" subsection as required under 21CFR 201.57(f)(10).

We have completed the review of this supplemental application and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the agreed upon labeling text and with the minor editorial revision listed below. Accordingly, this application is approved effective on the date of this letter.

Revise the PRECAUTIONS section, the "Geriatric Use" subsection, by adding the underlined phrase to the last sentence of the second paragraph of the subsection, to read as follows:

Geriatric Use
Clinical studies of CYKLOKAPRON did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an

elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

This drug is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function (See CLINICAL PHARMACOLOGY and DOSAGE AND ADMINISTRATION).

The final printed labeling (FPL) must be identical, and include the minor editorial revision indicated, to the labeling submitted May 14, 2001. Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug product.

Please submit the copies of final printed labeling (FPL) electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format – NDA* (January 1999). Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designed "FPL" for approved NDA 19-181/S-015. Approval of this submission by FDA is not required before the labeling is used.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, call Karen Oliver, Regulatory Project Manager, at (301) 827-7457.

Sincerely,

Victor F. C. Raczkowski, M.D., M.Sc.
Acting Division Director
Division of Gastrointestinal and Coagulation Drug Products
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Victor Raczkowski
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